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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,191	03/11/2004	Russell G. Kerr	6818-58-2	5136
30448	7590	06/18/2007	EXAMINER	
AKERMAN SENTERFITT			RAMIREZ, DELIA M	
P.O. BOX 3188			ART UNIT	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/798,191

Applicant(s)

KERR ET AL.

Examiner

Delia M. Ramirez

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION..

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-19 and 21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14-19 is/are allowed.
- 6) ☒ Claim(s) 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 3/11/2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

Claims 14-19, 21 are pending.

Applicant's amendment of claims 14, 16 addition of claim 21, and amendment of the first paragraph of the specification, as submitted in a communication filed on 4/6/2007 are acknowledged.

The Examiner contacted Mr. Nicholas Zachariades on 5/1/2007 but no agreement could be reached to place the application in condition for allowance.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112, Second Paragraph

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claims 14-20 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention due to the recitation of the term "elisabethatriene cyclase".
3. Applicant argues that claim 14 has been amended to clarify what is the intended meaning of the phrase. With regard to claim 21, Applicant argues that the specification defines in paragraph [11] the term such that the definition is enough for the skilled artisan to determine how to avoid infringement of the claim.
4. In view of Applicant's amendment which provides additional structural characteristics defining the enzyme, this rejection as it applies to claims 14-20 is hereby withdrawn. With regard to claim 21, it is noted that the specification's definition of the term states that the intended meaning of the term is a purified enzyme that can be isolated (isolatable) from *P. elisabethae*, has the ability to cyclize GGPP, and can have any level of structural similarity to the *P. elisabethae* enzyme disclosed in the specification.

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Thus, in view of this definition, the term has been interpreted to encompass any enzyme that can cyclize GGPP. The definition set forth in the specification does not provide any structural or origin limitation.

As such, no structural or origin limitations are encompassed by the term.

Claim Rejections - 35 USC § 112, First Paragraph

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. New claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. An extensive discussion of this rejection has been provided in the Non Final action mailed on 12/6/2006. This rejection as it relates to claim 21 is necessitated by amendment and it is applied to the instant claim for the reasons of record and those set forth below.

7. New claim 21 is directed to a method of cyclizing any substrate with a genus of enzymes that catalyze cyclization of GGPP. As discussed above, the definition provided in paragraph [11] of the term "elisabethatriene cyclase" does not place any limitations on the structure or origin of the enzyme. The only functionality clearly defined in the specification for the term is that of a catalyst of the cyclization of GGPP. See Claim Rejections under 35 USC 112, second paragraph, for extensive discussion. While Applicant argues that this definition limits the genus of species to those sharing structural and functional similarities to the purified native form of elisabethatriene cyclase isolatable from *P. elisabethae*, it is reiterated herein that the definition provided does not put any limitations with regard to the structure or origin of the recited enzyme. The term "isolatable" does not limit the source since the term means "can be isolated". This language does not exclude other sources for the enzyme. The term "having similar

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structure (e.g., sharing 65%, 70%, 75%, 80%, 85%, 90....or more sequence identity)” as set forth in paragraph [11] cannot be construed as limiting the structure of the genus of enzymes recited in view of the fact that (1) there is no complete sequence associated with the only *P. elisabethae* enzyme described such that one could make a determination of sequence identity, (2) there is no threshold regarding sequence identity below which an enzyme that can cyclize GGPP would not be encompassed by the claims, and (3) the term “e.g., 65....” is exemplary language which does not define a lower limit in sequence identity for the genus of enzymes recited.

As indicated in the Non Final action mailed on 12/6/2006, while the specification of the instant application partially discloses the structure of one species of the genus of enzymes recited, it provides no information as to the structural elements required in any enzyme which can cyclized GGPP or any additional species by any relevant, identifying characteristics or properties other than by functionality (i.e., cyclization of GGPP). The claim encompasses a large genus of enzymes which are structurally unrelated. A sufficient written description of a genus of products may be achieved by a recitation of a representative number of products defined by their structure (e.g., amino acid sequence) or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, there is no structural feature which is representative of all the members of the genus of enzymes recited in the claim, and there is no information as to a correlation between structure and function. Furthermore, while one could argue that the single enzyme species disclosed is representative of the structure of all the members of the genus of enzymes recited, it is noted that the art teaches several examples of how even small changes in structure can lead to changes in function. See the teachings of Witkowski et al., Seffernick et al. and Branden et al. previously discussed. Therefore, for the reasons set forth above and those of record, one cannot reasonably conclude that the specification provides adequate description of the genus of enzymes required in the method of claim 21.

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8. New claim 21 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of cyclizing GGPP, GGPP analogues, 3-PhGGPP, FPP, FPP isomers, FPP analogues, and phosphoisoprenoids with a polypeptide which (1) comprises SEQ ID NO: 1, 2, 3, 4, and 5, (2) has an isoelectric point of 5.1, (3) a molecular weight of 47 KDa, and (4) has the ability to cyclize geranyl geranyl diphosphate to elisabethatriene, does not reasonably provide enablement for a method for cyclizing any substrate with any enzyme which can cyclize GGPP. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. An extensive discussion of this rejection has been provided in the Non Final action mailed on 12/6/2006. This rejection as it relates to claim 21 is necessitated by amendment and it is applied to the instant claim for the reasons of record and those set forth below.

9. New claim 21 is so broad as to encompass a method of cyclizing any substrate with any enzyme that catalyze cyclization of GGPP. As discussed above, the definition provided in paragraph [11] of the term "elisabethatriene cyclase" does not place any limitations on the structure or origin of the enzyme. The specification partially discloses the structure of a single enzyme having the recited enzymatic activity. However, the specification fails to provide any clue as to (1) the structures of other proteins that can cyclize GGPP, (2) whether the partial fragments disclosed (SEQ ID NO: 1-5) are essential for that enzymatic activity, either individually or as a set, or (3) the structural elements required in any protein having the required functional characteristics. There is no information or guidance as to the amino acids in the enzyme disclosed which are associated with the required enzymatic activity. Neither the specification nor the art provide a correlation between structure and activity such that one of skill in the art can envision the structure of any protein having the recited enzymatic activity. The art, as evidenced by Witkowski et al., Seffernick et al. and Branden et al. previously discussed, clearly teaches the unpredictability of isolating proteins of similar function based solely on structural homology in view of

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the fact that even minor structural modifications can have a significant effect on function. Since neither the specification nor the art provides any guidance as to how to select/identify/isolate structural variants of the only *P. elisabethae* enzyme described in the specification which would have the ability to cyclize GGPP, one of skill in the art would have to test an essentially infinite number of proteins and determine whether they can cyclize GGPP. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claim.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by Peters et al. (Biochemistry 39:15592-15602, 2000). As indicated above, claim 21 is directed to a method which comprises the step of obtaining an enzyme which can cyclize GGPP, mixing said enzyme with a substrate that can be cyclized by the enzyme, and cyclizing the substrate. See extensive discussion above regarding the term “elisabethatriene cyclase”. Peter et al. teach the cyclization of GGPP with an enzyme which cyclizes GGPP (abietadiene synthase; Scheme 1, page 15593, (1) is GGPP; Experimental Procedures, Enzyme assays and inhibition studies, page 15594, right column). Therefore, the method of Peters et al. anticipate the instant claim as written.

Allowable Subject Matter

12. Claims 14-19 appear to be allowable over the prior art of record.

Conclusion

13. Applicant's amendment adding claim 21 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

14. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone

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are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

A handwritten signature in black ink, appearing to read 'DR', with a horizontal line extending to the right.

Delia M. Ramirez, Ph.D.
Primary Patent Examiner
Art Unit 1652

DR
June 1, 2007